REMARKS / ARGUMENTS

Claims 1-7 are pending in the application and stand rejected. By the foregoing amendment, the applicants have amended claims 1, 4 and 6 and canceled claim 3. Claims 8-11 are new. No new matter is added by the amendments. Support for the amendments can be found in the specification as filed. In view of the foregoing amendments and following discussion, the applicants submit that all pending claims are in condition for allowance.

On page 2 of the Office Action the Examiner rejected claims 1-2 for not being enabled for all active ingredients. The applicants have overcome this rejection by the foregoing amendment to claim 1. The applicants submit amended claim 1 is enabled. Accordingly the applicants request the Examiner to withdraw the rejection.

On page 6 the Examiner rejected claims 1-4 and 6 under 35 U.S.C. § 103(a) as being unpatentable over Adjei et al., (U.S. Pat. No. 6,261,539). The applicants respectfully traverse the rejection. Adjei does not disclose or suggest the invention of amended claim 1.

Amended claim 1 recites a formulation comprising water in an amount of about 0.13 to about 0.18 percent (w/w) of the product formulation, at least one HFA as a propellant, one or more excipients, and active ingredients albuterol sulfate and ipratropium bromide wherein the active ingredients of the formulation are suspended.

Adjei teaches only a single active ingredient formulation. There is no teaching or suggestion of a combined albuterol sulfate / ipratropium bromide suspension formulation.

Moreover, the Examiner has not interpreted the data in the Declaration of George DeStefano ("DeStefano Declaration") properly. The Examiner stated that the claimed range of water of 0.13 to 0.18% in rejected claim 1 is within the disclosed range of 0.03 to 0.2% for water in Adjei and thus a prima facie case of obviousness exists. Furthermore, the Examiner found unpersuasive the previously made argument that the instantly claimed range of 0.13 to 0.18% water resulted in unexpected results. Specifically, the Examiner noted that no unexpected results were shown because "there is no significant difference between, for example, 115.13, 118.31 and 119.26 [µg] (for albuterol) . . . [and] even less distinction shown between 20.56, 20.22 and 21.31 [µg] (for ipratropium)" (pages 17-18 of the instant Office Action). The applicants note the Examiner is incorrectly comparing the amount of active ingredient (i.e., albuterol or ipratropium) present in one actuation event from three different cans, each can having a different water content (i.e., 1500, 2500 or 3500 ppm of water). Instead, the Examiner should compare, as the

applicants have previously done to show the unexpected results, the reproducibility in a single "can" containing a specific water content (i.e., 2500 ppm) to repeatedly provide the same amount of the active ingredients released from the same "can" over a series of single actuation events as compared to a "can" containing a different water content (i.e., 1500 ppm). For the purpose of showing unexpected results, it is irrelevant whether "cans" containing different water contents release the same or different amounts of the active ingredients. The applicants submit the unexpected result is not the difference in amounts of the active ingredients, released during one actuation event, between "cans" containing different water content, but rather the aforementioned reproducibility in a single can..

The applicants point to Figures 2 and 3 of Analytical Report AR-030012, submitted in the DeStefano Declaration, which show the results of the reproducibility for "cans" containing various water contents to release the same amount of albuterol sulfate (i.e., % of theory) during a single actuation event. Cans containing 1500 to 2500 ppm water content (equivalent to 0.15 to 0.25% w/w) clearly show significantly better reproducibility than those cans containing 1200 ppm water content (equivalent to 0.12% w/w) or less. Thus, unexpected results are apparent for cans containing a formulation comprising water in an amount of about 0.13 to about 0.18 percent (w/w).

Therefore, in light of the above discussion, the claimed water content range is not obvious in light of the disclosed range in Adjei. Thus, claim 1 is not obvious over Adjei and is therefore allowable. Claims 2, 4 and 6 which depend from claim 1 are also not obvious and are therefore allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejection.

On pages 8-12 the Examiner rejected claims 1-4 and 6 under 35 U.S.C. § 103(a) as being unpatentable over Lewis et al. (EP 1219293); over Ashurst et al. (U.S. Pat. No. 6,511,652); and over Keller et al. (U.S. Pat. 6,475,467). The applicants respectfully traverse the rejection. For reasons similar to those discussed above, and those discussed in previous responses incorporated herein by reference, none of the references teach or suggest the claimed invention. Lewis teaches a water content of 0.1% to 0.5%. Ashurst teaches a water content of at least 0.015% and exemplify formulations that contain 0.015% to 0.1% (col. 5, lines 24-39). Keller does not teach any range of water content, and only teaches a formulation comprising less than 1% water (col. 3, lines 55-67). None of the references teach or suggest the criticality of the claimed range of

water of the invention of amended claim 1 to result in a significantly better reproducibility for "cans" containing water content of 1500 to 2500 ppm to release the same amount of albuterol sulfate (i.e., % of theory) during each single actuation event. Therefore, claim 1 is not obvious over Lewis, Ashurst, or Keller and is therefore allowable. Claims 2, 4 and 6 which depend from claim 1 are also not obvious and are therefore allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejections.

On page 13 the Examiner rejected claims 5 and 7 under 35 U.S.C. § 103(a) as being unpatentable over Adjei et al. in view of Jager et al. (WO 9413262). The applicants respectfully traverse the rejection. The combination of the references does not result in the claimed invention. For reasons similar to those discussed above, Adjei does not teach or suggest the claimed water content of amended claim 1 that results in unexpected reproducibility as discussed above. Jager fails to cure the deficiency. Jager teaches an ipratropium MDI with a broad range of water content of 0 to 5% but does not teach or suggest the instantly claimed range that results in the unexpected reproducibility. Thus, the combination of Adjei and Jager does not result in amended claim 1. Therefore, claims 5 and 7 are not obvious over Adjei in view of Jager and are thus allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejection.

On page 14 the Examiner rejected claims 5 and 7 under 35 U.S.C. § 103(a) as being unpatentable over Lewis et al. in view of Jager et al. (WO 9413262). The applicants respectfully traverse the rejection. The combination of the references does not result in the claimed invention. For reasons similar to those discussed above, Lewis does not teach or suggest the claimed water content of amended claim 1 that results in unexpected reproducibility as discussed above. Jager fails to cure the deficiency. Jager teaches an ipratropium MDI with a broad range of water content of 0 to 5% but does not teach or suggest the instantly claimed range that results in unexpected reproducibility. Thus, the combination of Lewis and Jager does not result in amended claim 1. Therefore, claims 5 and 7 are not obvious over Lewis in view of Jager and are thus allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejection.

On page 16 the Examiner rejected claims 1-7 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-11 of U.S. Pat. No. 6,423,298 in view of Adjei et al. The applicants respectfully traverse the rejection. For reasons similar to those

discussed above, the claimed invention is not obvious over the combination of the references. The '298 patent discloses a water content ranging from 0.0001 to 10%. The shortcomings of the Adjei reference are discussed above. The combination of the references cannot teach a skilled artisan the claimed water content that results in unexpected reproducibility as discussed above. Therefore, the combination of the '298 patent and Adjei does not result in the claimed invention. Thus, claims 1, 2 and 4-7 are not obvious over the '298 patent in view of Adjei and are therefore allowable. Accordingly, the applicants respectfully request the Examiner to withdraw the rejection.

Applicants submit that all claims pending in the patent application are in condition for allowance. Accordingly, both reconsideration of this application and its swift passage to issuance are earnestly solicited. In the event there are any fees due and owing in connection with this matter, please charge same to our Deposit Account No. 11-0223.

Respectfully submitted,

Dated: February 13, 2009

s/Timothy X. Gibson/
Timothy X. Gibson, Reg. # 40,618
Attorney for Applicant

Gibson & Dernier LLP
900 Route 9 North
Woodbridge, NJ 07095
Tel: (732) 634-7634
Fax: (732) 634-6887

Patent Department
Boehringer Ingelheim Corp.
900 Ridgebury Road
P.O. Box 368
Ridgefield, CT 06877
Tel: (203) 798-9988